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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,373	09/28/2001	Patrick J. Muraca	5568/1042	3910

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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,373	MURACA, PATRICK J.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,9,10,12-15 and 17-38* is/are pending in the application.

4a) Of the above claim(s) *17-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9,10 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 4/18/05, are acknowledged. Amended claims 1, 9-10, and 13-15 are acknowledged.

Applicant's arguments, filed 4/18/05, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-2, 9-10, and 12-15 are herein under examination.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 9-10, and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schraml et al. (Clinical Cancer Research, August 1999, vol. 5, pages 1966-1975) in view of Lincoln et al. (P/N 6,553,317) and Lehman et al. (Cancer Research, February 2000, vol. 60, pages 1062-1069).

This rejection is necessitated by amendment.

Schraml et al. describe using tissue microarrays for gene amplification surveys in many different tissue types (title). Schraml et al. describe using a tissue microarray consisting of samples from 17 different tumor types with 397 individual tumors as well as 20 normal tissues arrayed in a single paraffin block (representing at least about 10% of the samples of the microarray, (diameter, 0.6mm) (abstract, Figure 1, page 1966, col. 2, last paragraph) which represents first and second locations having test tissue and a control oncology tissue microarray comprising a plurality of tissue samples (as stated in instant claim 1) as well as tissue samples greater than about 0.6 mm in diameter (as stated in instant claim 9). Schraml et al. describe retrieving selected regions of archival tissue blocks from tumor biopsies and small arrayed samples collected from potentially heterogeneous tumors that were analyzed with three previously well-studied oncogenes (page 1966, col. 2, second paragraph). Schraml et al. describe four array elements including cancerous sections from kidney, lung, breast, and colon tissues (Figure 2, B-E) which represent tissue samples that are substantially homogeneous cells, as stated in instant claim 13. Schraml et al. describe finding gene markers (i.e. CCND1) amplified in breast and other cancerous tissue types (abstract and page 1966, col. 2, first paragraph) which represent cancer-specific markers, as stated in instant claim 14. Schraml et al. describe hundreds of samples are precisely arrayed in a new paraffin block (page 1966, col. 2, second paragraph) which represents stably associated samples with distinct, known sublocations on a substrate, as stated in instant claim 1. Schraml et al. describe the precise positioning of tissue specimens to enable the generation of multiple replicate array blocks, each having samples from the same tissue specimens at identical coordinates (page 1970, col. 2) which represents allowing for side-by-side comparisons, as stated in instant claim 1. Schraml et al. describe using

frozen tissue samples from primary tumors (abnormally proliferating cells) and normal tissues (normally proliferating cells) and embedding the specimens in paraffin (page 1966, col. 2, third paragraph), as stated in instant claim 10. Schraml et al. describe using tumors in different stages and grades, including 96 breast tumors (page 1967, col. 1, second paragraph) which represents samples representing the progression of cancer from an early to an advanced stage, as stated in instant claims 1 and 12. Schraml et al. describe gene amplifications in different tumor types may confer diagnostic, prognostic, or therapeutic information for patient management (abstract) which represents information relating to each patient from which the tissue samples were obtained. Schraml et al. describe confirming and extending existing data with their results (abstract). It is further noted that the phrase "wherein the profile array substrate allows testing... in the control oncology tissue microarray" in instant claim 1 is an intended use that does not structurally limit the article of manufacture being claimed. Schraml et al. do not describe the substrate comprising an identifier providing access to a database comprising information relating to each patient from which the sample was obtained (instant claim 1), identifier causing a screen to be displayed with database links (instant claim 2), or wherein each tissue sample is from a patient treated with a drug (instant claim 15).

Lincoln et al. describe the use of bioinformatics to study genes differentially expressed or commonly expressed in different tissues or cell lines, such as normal (normally proliferating cells) and cancerous tissue (abnormally proliferating cells) (col. 1, lines 46-48). Lincoln et al. describe using a microarray with multiple samples (col. 3, lines 10-12) which represents a microarray with multiple locations. Lincoln et al. describe processing clones in groups on a 96-well plastic culture dish with each chamber/well comprising an indentation in the dish to separate

samples (col. 12, lines 20-25) which represents a stably associated samples with a distinct, known sublocation on a substrate. Lincoln et al. describe a barcode (identifier) for a lot or 96-well plate whose value is placed in a barcode field of a table in a database (col. 21, lines 30-41) which represents a substrate with an identifier that provides access to a database, as stated in instant claim 1. The samples in a plastic culture dish represent the sample (tissue or cells) being plastic-embedded. The information on the plastic culture dish, including precise sample location with lot and well information, is recorded for each sample and given to customers (col. 12, lines 29-36). Lincoln et al. describe using a relational database system for storing biomolecular sequence information with biological annotations (col. 2, lines 14-20) including information identifying (identifiers) sequences (col. 2, lines 28-34). Lincoln et al. describe a system allowing a user to selectively view information regarding sequences and reagent specifications (col. 2, lines 34-37) including a graphical user interface where a query is entered and matches between query and information is displayed (col. 2, lines 46-50), as stated in instant claim 2. Lincoln et al. describe using a relational database with tables (col. 15, lines 44-49) including a library table that includes records of each library in the gene expression database including an identifier (LibraryID) (col. 16, lines 7-9). Lincoln et al. describe the library table as having a "TissueID" attribute that is inherited from a "TissueSpecimen" table) and a "Tissue_Category" attribute as well as a "Lib_Description" attribute including information such as tissue name, disease state, patient age/gender (col. 16, lines 6-32) which represents information relating to each patient from which the tissue sample was obtained, as stated in instant claim 1. Lincoln et al. describe providing further information about a donor in a "MedicalHistory" table including information such as a problem such as breast cancer, breast, and neoplasm (col. 20, lines 33-40). Lincoln et

al. describe using a network to which the network server and clients are connected (col. 13, lines 3-9), as stated in instant claim 2. Lincoln et al. describe entries in various results screens may provide links to other information in the database (col. 23, lines 10-13) as stated in instant claim 2. Lincoln et al. describe each tissue specimen (as uniquely identified by TissueID) may have several diagnoses (i.e. normal, diseased, involved, cancerous) and each donor may provide multiple tissue specimens (col. 19, lines 35-67) which represent a progression of cancer from an early stage (i.e. normal) to an advanced stage (i.e. cancerous), as stated in instant claim 1. This act of providing multiple tissue specimens that are "cancerous" or "involved" is reasonably interpreted to include specimens from sites of a secondary metastasis of cancer. Lincoln et al. describe different development stages (col. 20, lines 13-14). Lincoln et al. describe studying or monitoring drug resistance in certain tissue (col. 5, lines 1-3). Lincoln et al. describe obtaining clones from a particular tissue (col. 4, lines 42-44) and using a set of clones on a microarray (col. 3, lines 10-12) which represents a microarray associated with tissue-material. Instant claim 1 states the profile array substrate "allows testing" and "comparison" but does not state that the testing and comparison are actually done on the profile array substrate itself. Lincoln et al. describe a given clone being compared contemporaneously, in parallel, against other clones in the internal and public databases (col. 5, line 65 to col. 6, line 4) which represents a simultaneous testing allowing for side-by-side comparisons of samples with a control, as stated in instant claim 1. Lincoln et al. describe comparing new sequences against existing (known) clone sequences to classify new clones as belonging to a known sequence already provided in the internal database (col. 7, lines 38-53). Although Lincoln et al. describe monitoring drug resistance, they do not describe each tissue sample is from a patient treated with a drug (instant claim 15).

Lehman et al. describe studying breast cancer patients for activity of exon and intron base changes in the p53 gene (abstract). Lehman et al. describe patient information, such as age (abstract). Lehman et al. describe gene studies in response to drug treatment (abstract). In Table 1, Lehman et al. describe various statistics of patients including the stage of breast cancer. Lehman et al. describe coding the samples from patients and entering the information into a database (page 1063, col. 1, first paragraph). Lehman et al. describe collecting blood (bodily fluid) from breast cancer patients for analyses (page 1063, col. 1, first paragraph). Lehman et al. describe using paraffin-embedded tumor specimens and samples from patients undergoing drug treatments (page 1068, col. 1, third paragraph), as stated in instant claims 10 and 15.

Lehman et al. state the identification of woman at risk for development of breast cancer will have important implications for the prevention of cancers, treatment strategies, and improved cure rates of these patients (page 1062, col. 2, third paragraph). Schraml et al. state their tissue microarray technology has the potential to greatly facilitate analysis of alterations in multiple tissue types (page 1966, col. 2, second paragraph). Schraml et al. state that tumor arrays are a powerful tool to rapidly screen different tumor types for gene copy number alterations (page 1966, col. 2, second paragraph). Schraml et al. state they have demonstrated the power of using minute arrayed tissue specimens for tumor screening (abstract). Lincoln et al. state bioinformatics includes methods to search databases quickly to analyze information and make predictions (col. 1, lines 31-37). Lincoln et al. state information manipulation has been made easier to perform and understand with the development of sophisticated computer database systems (col. 1, lines 62-64). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make improvements to existing gene expression techniques tied

to relational database systems, as stated by Lincoln et al, because even though these systems provide great power and flexibility in analyzing gene expression information, this technology is still in its infancy and further improvements are required to accelerate biological research for numerous applications (Lincoln et al. col. 2, lines 6-12). Therefore, it would have been obvious to one of ordinary skill in the art to improve efficiency of microarray analyses with minute frozen and bodily fluid samples from multiple cancer patients and multiple tumor types (as stated by Schraml et al. and Lehman et al.) and relaying such information of relational database systems (as stated by Lincoln et al.) in order to accelerate research and evaluation in therapeutic pharmaceutical development and other fields by providing broad amounts of important information to clients in an easy to perform and understand format, as stated by Lincoln et al. (col. 1, line 62 to col. 2, line 28).

Thus, Schraml et al., in view of Lincoln et al. and Lehman et al., motivate the instant claims.

Applicants submit that Lincoln et al, Schraml et al., and Lehman et al. do not teach all of the limitations of the instant invention. This statement is found unpersuasive as all of the limitations of the instant claims are described in the three prior art references, as summarized in the rejection above. Applicants state that Lincoln et al. and Lehman et al. describe extracting DNA or RNA, sequencing the DNA, and inputting sequence information into a database. It is noted that Schraml et al. describe most of the limitations in the amended claim set including tissue microarrays whereas further generic microarray computer analyses are described by Lincoln et al. and additional tumor specimen studies were described by Lehman et al. It is also noted that not all limitations in a 35 USC 103(a) rejection must come from one reference.

Applicants summarize sections of the Lehman et al. reference and the Schraml et al. reference. Applicants state that they have not invented the concept of using a tissue microarray, but rather claim a device which utilizes the benefits of microarray technology to compare a test tissue sample with a plurality of known tissue samples. It is acknowledged that Applicants have not invented the concept of using a tissue microarray. Applicants statement of claiming a device that compares a test tissue sample with a plurality of known tissue samples is confusing as the instant claims do not recite "known tissue samples". Applicants state that Schraml et al. do not suggest a database incorporated into the system. While Schraml et al. do not disclose a database, such a limitation is found obvious with the Lincoln et al. reference which discloses database and network usage with microarray technology. Applicants' arguments are deemed unpersuasive for the reasons given above.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

June 27, 2005

MARJORIE A. MORAN
PRIMARY EXAMINER
Marjorie A. Moran
6/30/05